

DOCKET NO: PHRM0022-100/00146

PATENT

IN THE CLAIMS:

This listing of claims will replace all prior versions, and listings, of claims in the application.

Please amend claims 31, 80 and 81.

Please cancel claims 30, 32, 33 and 83-87 without prejudice.

STATUS OF CLAIMS

1. **(withdrawn)** An isolated nucleic acid molecule comprising a nucleotide sequence that encodes a polypeptide comprising an amino acid sequence homologous to a sequence of SEQ ID NO:2; said nucleic acid molecule encoding at least a portion of nGPCR-1025.
2. **(withdrawn)** The isolated nucleic acid molecule of claim 1 comprising a sequence that encodes a polypeptide comprising a sequence of SEQ ID NO:2.
3. **(withdrawn)** The isolated nucleic acid molecule of claim 1 comprising a sequence homologous to a sequence of SEQ ID NO:1.
4. **(withdrawn)** The isolated nucleic acid molecule of claim 1 comprising a sequence of SEQ ID NO:1.
5. **(withdrawn)** The isolated nucleic acid molecule of claim 1 wherein said nucleic acid molecule is DNA.
6. **(withdrawn)** The isolated nucleic acid molecule of claim 1 wherein said nucleic acid molecule is RNA.
7. **(withdrawn)** An expression vector comprising a nucleic acid molecule of any one of claims 1 to 4.

DOCKET NO: PHRM0022-100/00146**PATENT**

8. **(withdrawn)** The expression vector of claim 7 wherein said nucleic acid molecule comprises a sequence of SEQ ID NO:1.
9. **(withdrawn)** The expression vector of claim 7 wherein said vector is a plasmid.
10. **(withdrawn)** The expression vector of claim 7 wherein said vector is a viral particle.
11. **(withdrawn)** The expression vector of claim 10 wherein said vector is selected from the group consisting of adenoviruses, baculoviruses, parvoviruses, herpesviruses, poxviruses, adeno-associated viruses, Semliki Forest viruses, vaccinia viruses, and retroviruses.
12. **(withdrawn)** The expression vector of claim 7 wherein said nucleic acid molecule is operably connected to a promoter selected from the group consisting of simian virus 40, mouse mammary tumor virus, long terminal repeat of human immunodeficiency virus, maloney virus, cytomegalovirus immediate early promoter, Epstein Barr virus, rous sarcoma virus, human actin, human myosin, human hemoglobin, human muscle creatine, and human metallothionein.
13. **(withdrawn)** A host cell transformed with an expression vector of claim 7.
14. **(withdrawn)** The transformed host cell of claim 13 wherein said cell is a bacterial cell.
15. **(withdrawn)** The transformed host cell of claim 14 wherein said bacterial cell is *E. coli*.

DOCKET NO: PHRM0022-100/00146**PATENT**

16. **(withdrawn)** The transformed host cell of claim 13 wherein said cell is yeast.
17. **(withdrawn)** The transformed host cell of claim 16 wherein said yeast is *S. cerevisiae*.
18. **(withdrawn)** The transformed host cell of claim 13 wherein said cell is an insect cell.
19. **(withdrawn)** The transformed host cell of claim 18 wherein said insect cell is *S. frugiperda*.
20. **(withdrawn)** The transformed host cell of claim 13 wherein said cell is a mammalian cell.
21. **(withdrawn)** The transformed host cell of claim 20 wherein mammalian cell is selected from the group consisting of chinese hamster ovary cells, HeLa cells, African green monkey kidney cells, human HEK-293 cells, and murine 3T3 fibroblasts.
22. **(withdrawn)** An isolated nucleic acid molecule comprising at least 10 nucleotides, said nucleic acid molecule comprising a nucleotide sequence complementary to at least a portion of a sequence of SEQ ID NO:1.
23. **(withdrawn)** The nucleic acid molecule of claim 22 wherein said molecule is an antisense oligonucleotide directed to a region of a sequence of SEQ ID NO:1.
24. **(withdrawn)** The nucleic acid molecule of claim 23 wherein said oligonucleotide is directed to a regulatory region of a sequence of SEQ ID NO:1.

DOCKET NO: PHRM0022-100/00146**PATENT**

25. **(withdrawn)** A composition comprising a nucleic acid molecule of any one of claims 1 to 4 or 22 and an acceptable carrier or diluent.
26. **(withdrawn)** A composition comprising a recombinant expression vector of claim 7 and an acceptable carrier or diluent.
27. **(withdrawn)** A method of producing a polypeptide that comprises a sequence of SEQ ID NO:2, and homologs thereof, said method comprising the steps of:
- a) introducing a recombinant expression vector of claim 8 into a compatible host cell;
 - b) growing said host cell under conditions for expression of said polypeptide; and
 - c) recovering said polypeptide.
28. **(withdrawn)** The method of claim 27 wherein said host cell is lysed and said polypeptide is recovered from the lysate of said host cell.
29. **(withdrawn)** The method of claim 27 wherein said polypeptide is recovered by purifying the culture medium without lysing said host cell.
30. **(canceled)**
31. **(currently amended)** ~~An isolated The polypeptide of claim 30 wherein said polypeptide comprises~~ comprising a sequence of SEQ ID NO:2.
32. **(canceled)**
33. **(canceled)**

DOCKET NO: PHRM0022-100/00146

PATENT

34. (canceled)

35. (currently amended) A composition comprising a polypeptide of claim ~~30~~ 80 and an acceptable carrier or diluent.

36. (withdrawn) An isolated antibody which binds to an epitope on a polypeptide of claim 30.

37. (withdrawn) The antibody of claim 36 wherein said antibody is a monoclonal antibody.

38. (withdrawn) A composition comprising an antibody of claim 36 and an acceptable carrier or diluent.

39. (withdrawn) A method of inducing an immune response in a mammal against a polypeptide of claim 30 comprising administering to said mammal an amount of said polypeptide sufficient to induce said immune response.

40. (withdrawn) A method for identifying a compound which binds nGPCR-1025 comprising the steps of:

- a) contacting nGPCR-1025 with a compound; and
- b) determining whether said compound binds nGPCR-1025.

41. (withdrawn) The method of claim 40 wherein the nGPCR-1025 comprises an amino acid sequence of SEQ ID NO:2.

42. (withdrawn) The method of claim 40 wherein binding of said compound to nGPCR-1025 is determined by a protein binding assay.

DOCKET NO: PHRM0022-100/00146**PATENT**

43. **(withdrawn)** The method of claim 40 wherein said protein binding assay is selected from the group consisting of a gel-shift assay, Western blot, radiolabeled competition assay, phage-based expression cloning, co-fractionation by chromatography, co-precipitation, cross linking, interaction trap/two-hybrid analysis, southwestern analysis, and ELISA.

44. **(withdrawn)** A compound identified by the method of claim 40.

45. **(withdrawn)** A method for identifying a compound which binds a nucleic acid molecule encoding nGPCR-1025 comprising the steps of:

- a) contacting said nucleic acid molecule encoding nGPCR-1025 with a compound; and
- b) determining whether said compound binds said nucleic acid molecule.

46. **(withdrawn)** The method of claim 45 wherein binding is determined by a gel-shift assay.

47. **(withdrawn)** A compound identified by the method of claim 45.

48. **(withdrawn)** A method for identifying a compound which modulates the activity of nGPCR-1025 comprising the steps of:

- a) contacting nGPCR-1025 with a compound; and
- b) determining whether nGPCR-1025 activity has been modulated.

49. **(withdrawn)** The method of claim 48 wherein the nGPCR-1025 comprises an amino acid sequence of SEQ ID NO:2.

DOCKET NO: PHRM0022-100/00146**PATENT**

50. **(withdrawn)** The method of claim 48 wherein said activity is neuropeptide binding.

51. **(withdrawn)** The method of claim 48 wherein said activity is neuropeptide signaling.

52. **(withdrawn)** A compound identified by the method of claim 48.

53. **(withdrawn)** A method of identifying an animal homolog of nGPCR-1025 comprising the steps:

a) comparing the nucleic acid sequences of the animal with a sequence of SEQ ID NO:1, and portions thereof, said portions being at least 10 nucleotides; and

b) identifying nucleic acid sequences of the animal that are homologous to said sequence of SEQ ID NO:1, and portions thereof, said portions comprising at least 10 nucleotides.

54. **(withdrawn)** The method of claim 53 wherein comparing the nucleic acid sequences of the animal with a sequence of SEQ ID NO:1, and portions thereof, said portions being at least 10 nucleotides, is performed by DNA hybridization.

55. **(withdrawn)** The method of claim 53 wherein comparing the nucleic acid sequences of the animal with a sequence of SEQ ID NO:1, and portions thereof, said portions being at least 10 nucleotides, is performed by computer homology search.

56. **(withdrawn)** A method of screening a human subject to diagnose a disorder affecting the brain or genetic predisposition therefor, comprising the steps of:

(a) assaying nucleic acid of a human subject to determine a presence or an absence of a mutation altering an amino acid sequence, expression, or biological activity

DOCKET NO: PHRM0022-100/00146**PATENT**

of at least one nGPCR-1025 that is expressed in the brain, wherein the nGPCR-1025 comprises an amino acid sequence of SEQ ID NO:2, and allelic variants thereof, and wherein the nucleic acid corresponds to a gene encoding the nGPCR-1025; and

(b) diagnosing the disorder or predisposition from the presence or absence of said mutation, wherein the presence of a mutation altering the amino acid sequence, expression, or biological activity of the nGPCR-1025 in the nucleic acid correlates with an increased risk of developing the disorder.

57. **(withdrawn)** A method according to claim 56, wherein the disease is a mental disorder.

58. **(withdrawn)** A method according to claim 56, wherein the assaying step comprises at least one procedure selected from the group consisting of:

a) comparing nucleotide sequences from the human subject and reference sequences and determining a difference of at least a nucleotide of at least one codon between the nucleotide sequences from the human subject that encodes a nGPCR-1025 reference sequence;

(b) performing a hybridization assay to determine whether nucleic acid from the human subject has a nucleotide sequence identical to or different from one or more reference sequences;

(c) performing a polynucleotide migration assay to determine whether nucleic acid from the human subject has a nucleotide sequence identical to or different from one or more reference sequences; and

(d) performing a restriction endonuclease digestion to determine whether nucleic acid from the human subject has a nucleotide sequence identical to or different from one or more reference sequences.

59. **(withdrawn)** A method according to claim 58 wherein the assaying step comprises: performing a polymerase chain reaction assay to amplify nucleic acid

DOCKET NO: PHRM0022-100/00146**PATENT**

comprising nGPCR-1025 coding sequence, and determining nucleotide sequence of the amplified nucleic acid.

60. **(withdrawn)** A method of screening for an nGPCR-1025 hereditary mental disorder genotype in a human patient, comprising the steps of:

(a) providing a biological sample comprising nucleic acid from said patient, said nucleic acid including sequences corresponding to alleles of nGPCR-1025; and

(b) detecting the presence of one or more mutations in the nGPCR-1025 allele;

wherein the presence of a mutation in a nGPCR-1025 allele is indicative of a hereditary mental disorder genotype.

61. **(withdrawn)** The method according to claim 60 wherein said biological sample is a cell sample.

62. **(withdrawn)** The method according to claim 60 wherein said detecting the presence of a mutation comprises sequencing at least a portion of said nucleic acid, said portion comprising at least one codon of said nGPCR-1025 allele, said portion comprising at least 10 nucleotides.

63. **(withdrawn)** The method according to claim 60 wherein said nucleic acid is DNA.

64. **(withdrawn)** The method according to claim 60 wherein said nucleic acid is RNA.

65. **(withdrawn)** A kit for screening a human subject to diagnose a mental disorder or a genetic predisposition therefor, comprising, in association:

DOCKET NO: PHRM0022-100/00146**PATENT**

(a) an oligonucleotide useful as a probe for identifying polymorphisms in a human nGPCR-1025 gene, the oligonucleotide comprising 6-50 nucleotides in a sequence that is identical or complementary to a sequence of a wild type human nGPCR-1025 gene sequence or nGPCR-1025 coding sequence, except for one sequence difference selected from the group consisting of a nucleotide addition, a nucleotide deletion, or nucleotide substitution; and

(b) a media packaged with the oligonucleotide, said media containing information for identifying polymorphisms that correlate with mental disorder or a genetic predisposition therefor, the polymorphisms being identifiable using the oligonucleotide as a probe.

66. **(withdrawn)** A method of identifying a nGPCR-1025 allelic variant that correlates with a mental disorder, comprising the steps of:

(a) providing a biological sample comprising nucleic acid from a human patient diagnosed with a mental disorder, or from the patient's genetic progenitors or progeny;

(b) detecting in the nucleic acid the presence of one or more mutations in an nGPCR-1025 that is expressed in the brain, wherein the nGPCR-1025 comprises an amino acid sequence of SEQ ID NO:2, and allelic variants thereof, and wherein the nucleic acid includes sequence corresponding to the gene or genes encoding nGPCR-1025;

wherein the one or more mutations detected indicates an allelic variant that correlates with a mental disorder.

67. **(withdrawn)** A purified and isolated polynucleotide comprising a nucleotide sequence encoding a nGPCR-1025 allelic variant identified according to claim 66.

68. **(withdrawn)** A host cell transformed or transfected with a polynucleotide according to claim 67 or with a vector comprising the polynucleotide.

DOCKET NO: PHRM0022-100/00146**PATENT**

69. **(withdrawn)** A purified polynucleotide comprising a nucleotide sequence encoding nGPCR-1025 of a human with a mental disorder;

wherein said polynucleotide hybridizes to the complement of a sequence of SEQ ID NO:1 under the following hybridization conditions:

(a) hybridization for 16 hours at 42EC in a hybridization solution comprising 50% formamide, 1% SDS, 1 M NaCl, 10% dextran sulfate and

(b) washing 2 times for 30 minutes at 60EC in a wash solution comprising 0.1x SSC and 1% SDS; and

wherein the polynucleotide that encodes nGPCR-1025 amino acid sequence of the human differs from the sequence of SEQ ID NO:1 by at least one residue.

70. **(withdrawn)** A vector comprising a polynucleotide according to claim 69.

71. **(withdrawn)** A host cell that has been transformed or transfected with a polynucleotide according to claim 69 and that expresses the nGPCR-1025 protein encoded by the polynucleotide.

72. **(withdrawn)** A host cell according to claim 71 that has been co-transfected with a polynucleotide encoding the nGPCR-1025 amino acid sequence set forth in a sequence of SEQ ID NO:1 and that expresses the nGPCR-1025 protein having the amino acid sequence set forth in SEQ ID NO:2.

73. **(withdrawn)** A method for identifying a modulator of biological activity of nGPCR-1025 comprising the steps of:

- a) contacting a cell according to claim 72 in the presence and in the absence of a putative modulator compound;
- b) measuring nGPCR-1025 biological activity in the cell;

DOCKET NO: PHRM0022-100/00146**PATENT**

wherein decreased or increased nGPCR-1025 biological activity in the presence versus absence of the putative modulator is indicative of a modulator of biological activity.

74. **(withdrawn)** A method to identify compounds useful for the treatment of a mental disorder, said method comprising the steps of:

(a) contacting a composition comprising nGPCR-1025 with a compound suspected of binding nGPCR-1025;

(b) detecting binding between nGPCR-1025 and the compound suspected of binding nGPCR-1025;

wherein compounds identified as binding nGPCR-1025 are candidate compounds useful for the treatment of a mental disorder.

75. **(withdrawn)** A method for identifying a compound useful as a modulator of binding between nGPCR-1025 and a binding partner of nGPCR-1025 comprising the steps of:

(a) contacting the binding partner and a composition comprising nGPCR-1025 in the presence and in the absence of a putative modulator compound;

(b) detecting binding between the binding partner and nGPCR-1025;

wherein decreased or increased binding between the binding partner and nGPCR-1025 in the presence of the putative modulator, as compared to binding in the absence of the putative modulator is indicative a modulator compound useful for the treatment of a mental disorder.

76. **(withdrawn)** A method according to claim 74 or 75 wherein the composition comprises a cell expressing nGPCR-1025 on its surface.

DOCKET NO: PHRM0022-100/00146

PATENT

77. **(withdrawn)** A method according to claim 76 wherein the composition comprises a cell transformed or transfected with a polynucleotide that encodes nGPCR-1025.

78. **(withdrawn)** A method of purifying a G protein from a sample containing said G protein comprising the steps of:

- a) contacting said sample with a polypeptide of claim 1 for a time sufficient to allow said G protein to form a complex with said polypeptide;
- b) isolating said complex from remaining components of said sample;
- c) maintaining said complex under conditions which result in dissociation of said G protein from said polypeptide; and
- d) isolating said G protein from said polypeptide.

79. **(withdrawn)** The method of claim 78 wherein said sample comprises an amino acid sequence of SEQ ID NO:2.

Claim 80 **(currently amended)** ~~An isolated~~ The polypeptide of claim 32 ~~wherein said~~ wherein said comprising an amino acid sequence is at least 95% homologous to SEQ ID NO:2.

Claim 81 **(currently amended)** The isolated polypeptide of claim 32 80, wherein said polypeptide is a seven transmembrane receptor.

Claim 82 **(previously presented)** The isolated polypeptide of claim 81, wherein said seven transmembrane receptor is a G-protein coupled receptor.

Claim 83 **(canceled)**

Claim 84 **(canceled)**

DOCKET NO: PHRM0022-100/00146

PATENT

Claim 85 (canceled)

Claim 86 (canceled)

Claim 87 (canceled)